



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
09/057,016	4/7/98	Turpen	08 010087 US01
		EXAMINER	
		FOX	
ART UNIT	PAPER NUMBER		
	1649		12

DATE MAILED:

INTERVIEW SUMMARY

i-2

3-5

All participants (applicant, applicant's representative, PTO personnel):

(1) Albert C. Hallin 25,227 (3) David Fox

(2) Thomas Gallegos (32,692) (4) Lynette Smith

Date of Interview 6/3/98 (5) Richard Schwartz

Type: Telephonic Personal (copy is given to applicant applicant's representative).

Exhibit shown or demonstration conducted: Yes No If yes, brief description: pages 20, 33-35 of 07/31/881 parent application

Agreement was reached. was not reached.

Claim(s) discussed: 17

Identification of prior art discussed: Hemamoto et al

Description of the general nature of what was agreed to if an agreement was reached, or any other comments: Examiner indicated that based on previous mistaken assignment of 102(e) date by Examiner and correct 102(e) date of 1/94, results in Applicant becoming the senior party due to the effective filing date of 10/94 for new claim 17 as previously determined by the Examiner. TD to be filed. Requirement for new cash to be checked. Appl. rep. argued that MPEP § 2301.01 prevents claim interpretation by Examiner. Examiner stated that examination of instant spec + parents for determining support for the claim in instant application is appropriate. Examiner maintained that combination of fusion protein gene and "readthrough" or "dual vector system was not disclosed until 10/94 parent application. Pages 20, 33-35 of (A fuller description, if necessary, and a copy of the amendments, if available, which the examiner agreed would render the claims allowable must be attached. Also, where no copy of the amendments which would render the claims allowable is available, a summary thereof must be attached.) Feb 1989 parent submitted to support contention that both features were present. The Examiner stated that these pages

1. It is not necessary for applicant to provide a separate record of the substance of the interview.

Unless the paragraph above has been checked to indicate to the contrary, A FORMAL WRITTEN RESPONSE TO THE LAST OFFICE ACTION IS NOT WAIVED AND MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a response to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW.

2. Since the Examiner's interview summary above (including any attachments) reflects a complete response to each of the objections, rejections and requirements that may be present in the last Office action, and since the claims are now allowable, this completed form is considered to fulfill the response requirements of the last Office action. Applicant is not relieved from providing a separate record of the interview unless box 1 above is also checked.

Examiner Note: You must sign this form unless it is an attachment to another form.

David Fox

Manual of Patent Examining Procedure, Section 713.04 Substance of Interview must Be Made of Record

A complete written statement as to the substance of any face-to-face or telephone interview with regard to an application must be made of record in the application, whether or not an agreement with the examiner was reached at the interview.

§1.133 Interviews

(b) In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for response to Office action as specified in §§ 1.111, 1.135. (35 U.S.C.132)

§ 1.2. Business to be transacted in writing. All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete a two-sheet carbon interleaf Interview Summary Form for each interview held after January 1, 1978 where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks in neat handwritten form using a ball point pen. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below.

The Interview Summary Form shall be given an appropriate paper number, placed in the right hand portion of the file, and listed on the "Contents" list on the file wrapper. The docket and serial register cards need not be updated to reflect interviews. In a personal interview, the duplicate copy of the Form is removed and given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephonic interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the telephonic interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Serial Number of the application
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (personal or telephonic)
- Name of participant(s) (applicant, attorney or agent, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the claims discussed
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). (Agreements as to allowability are tentative and do not restrict further action by the examiner to the contrary.)
- The signature of the examiner who conducted the interview
- Names of other Patent and Trademark Office personnel present.

The Form also contains a statement reminding the applicant of his responsibility to record the substance of the interview.

It is desirable that the examiner orally remind the applicant of his obligation to record the substance of the interview in each case unless both applicant and examiner agree that the examiner will record same. Where the examiner agrees to record the substance of the interview, or when it is adequately recorded on the Form or in an attachment to the Form, the examiner should check a box at the bottom of the Form informing the applicant that he need not supplement the Form by submitting a separate record of the substance of the interview.

It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview:

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner. The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he feels were or might be persuasive to the examiner,
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete or accurate, the examiner will give the applicant one month from the date of the notifying letter or the remainder of any period for response, whichever is longer, to complete the response and thereby avoid abandonment of the application (37 CFR 1.135(c)).

Examiner to Check for Accuracy

Applicant's summary of what took place at the interview should be carefully checked to determine the accuracy of any argument or statement attributed to the examiner during the interview. If there is an inaccuracy and it bears directly on the question of patentability, it should be pointed out in the next Office letter. If the claims are allowable for other reasons of record, the examiner should send a letter setting forth his or her version of the statement attributed to him. If the record is complete and accurate, the examiner should place the indication "Interview record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.



US005618699A

#12

attach

United States Patent [19]
Hamamoto et al.

[11] Patent Number: **5,618,699**
[45] Date of Patent: **Apr. 8, 1997**

6/3/99
Review
[54] PLANT VIRUS VECTOR, PLASMID,
PROCESS FOR EXPRESSION OF FOREIGN
GENE AND PROCESS FOR OBTAINING
FOREIGN GENE PRODUCT

[75] Inventors: Hiroshi Hamamoto, Tsukuba;
Yoshinori Sugiyama, Odawara;
Noriaki Nakagawa, Odawara; Eiji
Hashida, Odawara; Suguru
Tsuchimoto, Odawara; Noriyuki
Nakanishi, Zama; Yuji Matsunaga,
Osaka; Yoshimi Okada, Matsudo, all of
Japan

[73] Assignee: Kanebo Limited, Tokyo, Japan

[21] Appl. No.: **313,127**

[22] PCT Filed: **Mar. 31, 1993**

[86] PCT No.: **PCT/JP93/00408**

§ 371 Date: **Nov. 30, 1994**

§ 102(e) Date: **Nov. 30, 1994**

[87] PCT Pub. No.: **WO93/20217**

PCT Pub. Date: **Oct. 14, 1993**

[30] Foreign Application Priority Data

Mar. 31, 1992	[JP]	Japan	4-108628
Jun. 22, 1992	[JP]	Japan	4-188744
Dec. 8, 1992	[JP]	Japan	4-351970

[51] Int. Cl⁶ C12N 15/40; C12N 15/62;
C12N 15/82; C12N 15/83

[52] U.S. Cl. 435/69.7; 435/69.1; 435/70.1;
435/172.3; 435/235.1; 435/320.1; 536/23.72;
800/205; 800/DIG. 43; 800/DIG. 44

[58] Field of Search 435/69.1, 70.1,
435/172.3, 235.1, 320.1, 69.7; 536/23.72;
800/205, DIG. 43, DIG. 44

[56] References Cited

FOREIGN PATENT DOCUMENTS

WO8908145 9/1989 WIPO .

OTHER PUBLICATIONS

Skuzeski et al. 1991. J. Mol. Biol. 218:365-373.
Takamatsu et al. 1983. Nucleic Acids Research II(11):
3767-3778.
Ugaki et al. 1991. J. Gen. Virol. 72:1487-95.
Solis et al. 1990. Virology 177:553-558.
Isomura et al. 1991. J. Gen. Virol. 72:2247-2249.
Alonso et al. J. Gen. Virol. 72: 2875-2884.
Takamatsu et al., The EMBO Journal vol. 6, No. 2, pp.
307-311 (1987).
Saito et al., Virology 176, pp. 329-336 (1990).
Meshi et al., Proc. Natl. Acad. Sci. USA, vol. 83, pp.
5043-5047 (1986).
Ahlquist et al., Mol. Cell. Biol. vol. 4 No. 12, pp. 2876-2882
(1984).
Rosa, Cell. vol. 16 pp. 815-825 (1979).
Joshi et al., "Strategies for Expression of Foreign Genes in
Plants—Potential Use of Engineered Viruses", FEBS Letter,
281(1,2):1-8 (1991).
Takamatsu et al., "Production of Enkephalin in Tobacco
Protoplasts Using Tobacco Mosaic Virus RNA Vector",
FEBS Letter, 269(1):73-76 (1990).
Skuzeski et al. 1990. Plant Mol. Biol. 15: 65-79.

Primary Examiner—David T. Fox

Attorney, Agent, or Firm—Sughrue, Mion, Zinn, Macpeak &
Seas

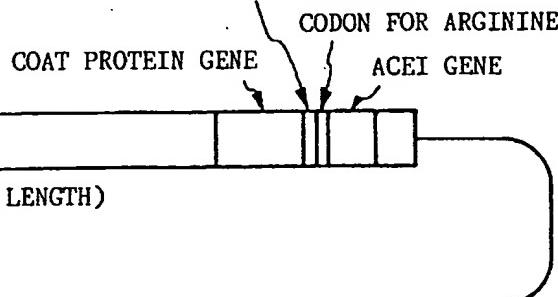
[57] ABSTRACT

The present invention relates to a plant virus vector comprising a foreign gene linked downstream of a coat protein gene of tobacco mosaic virus via a nucleotide sequence which cause the readthrough, and a plasmid which is transcribed to provide the vector, as well as a process for expression of a foreign gene in a plant by inoculating the plant with the vector.

In addition, the present invention relates to a process for efficiently recovering a foreign gene product produced in a plant as virions.

25 Claims, 9 Drawing Sheets

SEQUENCE CAUSING READTHROUGH



**PLANT VIRUS VECTOR, PLASMID,
PROCESS FOR EXPRESSION OF FOREIGN
GENE AND PROCESS FOR OBTAINING
FOREIGN GENE PRODUCT**

FIELD OF THE INVENTION

The present invention relates to introduction of a foreign gene into a plant using a plant virus vector, improvement of plant properties and expression of a foreign gene throughout a whole plant, and a process for simply and efficiently obtaining a foreign gene product.

BACKGROUND OF THE INVENTION

It is known that plant viruses represented by tobamovirus, after infecting a plant, proliferate in the plant and rapidly spread systemically throughout the plant while producing viral coat protein in large amounts.

So far, some gene engineering systems for these plant viruses have been constructed and some attempts have been carried out to introduce a foreign gene into a plant using said systems. For example, there is a process wherein a coat protein gene is replaced with a foreign gene (Takamatsu et al, *EMBO J.*, 6:307-311 (1987)), and a process wherein a coat protein gene and a foreign gene are directly joined so as to produce a fused protein (Takamatsu et al, *FEBS Lett.*, 269:73-76 (1990)).

However, all of the plant viruses used in these known processes have a drawback in that they do not spread systemically in a plant (i.e., they do not have systemic infectivity), and thus, it is impossible to introduce a useful property and to produce a useful protein throughout a whole plant.

For a plant virus to exhibit systemic infectivity, particle formation with wild type coat protein is essential (Saito et al, *Virology*, 176:329 (1990)). As to existing plant virus vectors, since the coat protein is not produced (replacement-type vector), or the coat protein is in the form of a fused protein, resulting in a big change in properties (direct-joining type vector); then particles cannot be formed and systemic infectivity is not exhibited.

In addition, where existing plant virus vectors are used to express a foreign gene, it is very difficult to isolate and purify the foreign gene product from the plant into which the foreign gene was introduced.

The reason is that to establish (1) simple apparatus and economy, (2) high recovery, (3) high purity and (4) good reproduction, which are the goals of isolation and purification, a combination of operations, such as differential precipitation, desalting, concentration, and various chromatographies is essential; however, a series of these operations usually takes one-half to one month to complete, and they are often time- and labor-consuming. Even assuming these operations are simple and rapid, a plant includes proteins whose properties, such as molecular weight, isoelectric point, affinity to a solvent, are similar to those of the foreign gene product; and therefore it is difficult to prevent loss of the foreign gene product during the isolation and purification process. Thus, high recovery of the foreign gene product is not expected.

SUMMARY OF THE INVENTION

The purpose of the present invention is to provide plant virus vectors having the ability to systemically infect a whole plant; plasmids, which are transcribed to provide said

plant virus vectors; and a process for expressing a foreign gene throughout a whole plant by inoculating said plant virus vector into a plant.

5 In addition, a process for simply and efficiently obtaining a foreign gene product produced in a plant is provided.

To accomplish the above-mentioned purposes, the present inventors use plant virus vector wherein a foreign gene is linked downstream of a coat protein gene of a plant virus via a nucleotide sequence that causes readthrough (Skuzeski et al, *J. Mol. Biol.*, 218:365-373 (1991)); a plasmid that is transcribed to provide said plant virus vector; and infection throughout a whole plant (systemic infectivity) by inoculating said plant virus vector into a plant so as to express the foreign gene throughout the whole plant. It was also found that introduction of a useful property into a whole plant and the production of a useful protein in a whole plant are possible, and thus, the present invention has been achieved.

10 In addition the present inventors found that when a foreign gene product is recovered from a plant, the foreign gene product can be easily and efficiently recovered as viral particles.

Prior to explaining the constituent features of the present invention, the terms used in the specification are explained as follows:

15 Plant virus vector: a replicable recombinant product obtainable by introducing a foreign gene into a DNA or RNA sequence in a plant virus.

Readthrough: In translation of an RNA to a protein, a phenomenon wherein the translation does not stop at a stop codon, and sometimes continues to the next stop codon. This readthrough phenomenon is caused by a nucleotide sequence near the stop codon.

20 Plant: in addition to an individual plant (a plant consisting of leaves, stem and roots); plant cells, callus, protoplast, as well as adventitious buds, adventitious roots and somatic embryos, derived from callus, are included, which are used as hosts for a plant virus.

25 Wild coat protein: A protein essential for formation of virions. Although it is usually called coat protein, in the present invention, to distinguish it from a coat protein in a fused protein, it is described as wild coat protein.

30 Fused protein: A protein wherein a foreign gene product is joined to the C-terminal of a coat protein, or a protein wherein a part of a coat protein is replaced with a foreign gene product.

35 Virion: A viral genome covered with a coat protein.

40 As plant viruses used in the present invention, there are mentioned a group belonging to DNA viruses, such as Caulimovirus and Geminivirus; and a group belonging to RNA viruses, such as Tobamovirus, Bromovirus and Cucumovirus. Particular virus species include Cauliflower mosaic virus belonging to Caulimovirus; Tomato golden mosaic virus belonging to Geminivirus; Tobacco mosaic virus belonging to Tobamovirus; Bromo mosaic virus belonging to Bromovirus; and Cucumber mosaic virus belonging to Cucumovirus.

45 Foreign genes used in the present invention include genes for peptides having a pharmacological or physiological activity; genes for proteins which provide stress resistance or pest resistance to a plant; and genes for proteins which change flower shape or color; more particularly, genes coding for enkephalins, calcitonins, corticotropins, human epidermal growth factor, and angiotensin converting enzyme inhibitor (ACEI) peptides having hypotensive action, as shown in the following Table 1.

-continued

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(i i) MOLECULE TYPE: peptide

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:10:

```

A l a   V a l   P r o   T y r   P r o   G l n   A r g
      5

```

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 6 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(i i) MOLECULE TYPE: peptide

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:11:

```

T h r   T h r   M e t   P r o   L e u   T r p
      5

```

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(i i) MOLECULE TYPE: peptide

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:12:

```

P h e   P h e   V a l   A l a   P r o
      5

```

We claim:

1. A plant virus vector comprising a viral assembly origin and a foreign protein gene linked downstream of a coat protein gene of a Tobamovirus via a nucleotide sequence of a Tobamovirus which causes readthrough, such that upon expression of the vector in a plant, the coat protein and a fusion protein of the coat protein and the foreign protein are systemically produced in the plant.

2. The plant virus vector according to claim 1, wherein part of the coat protein gene is lacking or replaced.

3. The plant virus vector according to claim 1, wherein the nucleotide sequence which causes readthrough is UAG-CAAUUA or the corresponding DNA sequence TAG-CAATTAA, UAACAAUUA or the corresponding DNA sequence TAACAAATTAA, UGACAAUUA or the corresponding DNA sequence TGACAAATTAA, or UAGCARYYA or the corresponding DNA sequence TAGCARYYA, wherein the italicized lettering indicates a stop codon, R is A or G, and Y is C, U or T.

4. A plasmid comprising the plant virus vector according to claim 1.

5. The plasmid according to claim 4, wherein the nucleotide sequence which causes readthrough is UAGCAAUUA or the corresponding DNA sequence TAGCAATTAA, UAA-CAAUUA or the corresponding DNA sequence TAA-CAATTAA, UGACAAUUA or the corresponding DNA sequence TGACAAATTAA, or UAGCARYYA or the corresponding DNA sequence TAGCARYYA, wherein italicized lettering indicates a stop codon, R is A or G, and Y is C, U or T.

45

50

55

sponding DNA sequence TAGCARYYA, wherein italicized lettering indicates a stop codon, R is A or G, and Y is C, U or T.

6. The plasmid according to claim 4, wherein said plasmid comprises cDNA to said Tobamovirus and a promoter for transcribing said cDNA upstream from said cDNA.

7. The plasmid according to claim 6, wherein the nucleotide sequence which causes readthrough is UAGCAAUUA or the corresponding DNA sequence TAGCAATTAA, UAA-CAAUUA or the corresponding DNA sequence TAA-CAATTAA, UGACAAUUA or the corresponding DNA sequence TGACAAATTAA, or UAGCARYYA or the corresponding DNA sequence TAGCARYYA, wherein italicized lettering indicates a stop codon, R is A or G, and Y is C, U or T.

8. The plasmid according to claim 6, wherein the promoter is the PM promoter or the T7 promoter.

9. A process for systemically expressing a fusion protein of a coat protein and a foreign protein in a plant comprising the steps of:

- (a) inoculating a plant with a plant virus vector, wherein the plant virus vector comprises a viral assembly origin and a foreign protein gene linked downstream of a coat protein gene of a Tobamovirus via a nucleotide sequence of a Tobamovirus which causes readthrough, such that upon expression of the vector in the plant, the

17

coat protein and the fusion protein are systemically produced in the plant; and

(b) expressing the fusion protein systemically in the plant.

10. The process according to claim 9, wherein a part of the coat protein gene is lacking or replaced.

11. The process according to claim 9 wherein the nucleotide sequence which causes readthrough is UAGCAAUUA or the corresponding DNA sequence TAGCAATTAA, UAACAAUUA or the corresponding DNA sequence TAA-CAATTAA, UGACAAUUA or the corresponding DNA sequence TGACAATTAA, or UAGCARYYA or the corresponding DNA sequence TAGCARYYA, wherein italicized lettering indicates a stop codon, R is A or G, and Y is C, U or T.

12. The process according to claim 9, wherein the plant is tobacco or tomato.

13. A process for producing a fusion protein of a coat protein and a foreign protein in a plant comprising the steps of:

(1) inoculating a plant with a plant virus vector, wherein the plant virus vector comprises a viral assembly origin and a foreign protein gene linked downstream of a coat protein gene of a Tobamovirus via a nucleotide sequence of a Tobamovirus which causes readthrough, such that upon expression of the vector in a plant, the coat protein and the fusion protein of the coat protein and the foreign protein are systemically produced in the plant;

(2) recovering virions from the plant; and

(3) isolating the fusion protein from the virions.

14. The plant virus vector according to claim 2, wherein the coat protein gene has the sequence of SEQ ID NO:5.

15. The plant virus vector according to claim 2, wherein the coat protein gene has the sequence of SEQ ID NO:7.

16. A virion particle comprising a coat protein of a Tobamovirus and a fusion protein of the coat protein and a foreign protein.

17. A process for systemically expressing a fusion protein of a coat protein of a Tobamovirus and a foreign protein in a plant comprising the steps of:

(a) inoculating a plant with a plant virus vector, such that upon expression of the vector in a plant, the coat protein of a Tobamovirus and the fusion protein of the coat protein and the foreign protein are systemically produced in the plant; and

(b) expressing the fusion protein systemically in the plant.

18. A tobacco mosaic viral (TMV) vector comprising a TMV assembly origin and a foreign protein gene linked downstream of a TMV coat protein gene via a TMV nucleotide readthrough sequence, such that upon expression of the vector in a plant, the TMV coat protein and a fusion protein of the coat protein and the foreign protein are systemically produced in the plant, wherein said readthrough sequence is from a 130/180K protein gene, UAGCAAUUA or the corresponding DNA sequence TAA-CAATTAA, UAACAAUUA or the corresponding DNA

18

sequence TAACAATTAA, UGACAAUUA or the corresponding DNA sequence TGACAATTAA, or UAGCARYYA or the corresponding DNA sequence TAGCARYYA, wherein italicized lettering indicates a stop codon, R is A or G, and Y is C, U or T.

19. The vector according to claim 18, wherein a part of the coat protein gene is lacking or replaced.

20. A plasmid comprising the plant virus vector of claim 18.

21. The plasmid according to claim 20, wherein the plasmid further comprises a promoter, wherein said promoter is the PM promoter or the T7 promoter.

22. A process for systemically expressing a fusion protein of a TMV coat protein and a foreign protein in a plant comprising the steps of:

(a) inoculating a plant with a TMV vector comprising a TMV assembly origin and a foreign protein gene linked downstream of a TMV coat protein gene via a TMV readthrough sequence, such that upon expression of the vector in the plant, the TMV coat protein and the fusion protein are systemically produced in the plant, wherein said readthrough sequence is from a 130/180K protein gene, UAGCAAUUA or the corresponding DNA sequence TAGCAATTAA, UAACAAUUA or the corresponding DNA sequence TAACAATAA, TGACAA-UUA or the corresponding DNA sequence TGA-CAATTAA, or UAGCARYYA or the corresponding DNA sequence TAGCARYYA, wherein italicized lettering indicates a stop codon, R is A or G, and Y is C, U or T, and

(b) expressing the fusion protein systemically in the plant.

23. The process according to claim 22, wherein a part of the coat protein gene is lacking or replaced.

24. A process for producing a fusion protein of a TMV coat protein and a foreign protein in a plant comprising the steps of:

(1) inoculating a plant with a TMV vector comprising a TMV assembly origin and a foreign protein linked downstream of a TMV coat protein gene via a readthrough sequence, such that upon expression of the vector in the plant, the TMV coat protein and a fusion protein of the coat protein and the foreign protein are systemically produced in the plant, wherein said readthrough sequence is from a 130/180K protein gene, UAGCAAUUA or the corresponding DNA sequence TAGCAATTAA, UAACAAUUA or the corresponding DNA sequence TAACAATAA, TGACAAUUA or the corresponding DNA sequence TGACAATTAA, or UAG-CARYYA or the corresponding DNA sequence TAG-CARYYA, wherein italicized lettering indicates a stop codon, R is A or G, and Y is C, U or T;

(2) recovering virions from the plant; and

(3) isolating the fusion protein from the virions.

25. The process according to claim 24, wherein a part of the coat protein gene is lacking or replaced.

* * * * *

for a period of 3-months due to possible interference. This allows a period of 2 months to complete any action needed. At the end of this 2-month period, the application must either be released to the Publishing Division or be withdrawn from issue.

(6/3/95)
Interview

When an application is found claiming an invention for which claims are to be suggested to other applications already involved in interference, to form another interference, the primary examiner, after obtaining the consent of the administrative patent judge in charge of the interference, borrows the last named applications from the Service Branch of the Board of Patent Appeals and Interferences. In case the application is to be added to an existing interference, the primary examiner need only send the application and form PTO-850 (illustrated in MPEP § 2309.02) properly filled out as to the additional application and identifying the interference, to the administrative patent judge in charge of the interference who will determine the action to be taken. Also, see MPEP § 2342 and § 2364.01.

¶ 23.08 Suggestion of Claims – Application in Issue

This application has been withdrawn from issue for consideration of a potential interference based on the claims suggested in this action.

Examiner Note:

1. If a conflicting application is in issue, it should be withdrawn using form paragraphs 10.01 or 10.02 prior to suggesting claims for interference.
2. Either form paragraph 23.04 or 23.09 must be used in conjunction with this paragraph.

¶ 23.19 Foreign Priority Not Substantiated

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Examiner Note:

This paragraph may be used when claims are suggested to applicant from either an application or a patent and applicant has a claim for priority, but has not filed a translation of the priority document.

2306 Interference Between an Application and a Patent

37 CFR 1.606. Interference between an application and a patent; subject matter of the interference.

Before an interference is declared between an application and an unexpired patent, an examiner must determine that there is interfering subject matter claimed in the application and the patent which is patentable to the applicant subject to a judgment in the interference. The interfering subject matter will be defined by one or more counts. The application must contain, or be amended to contain, at least one claim that is patentable over the prior art and corresponds to each count. The claim in the application need not be, and most often will not be, identical to a claim in the patent. All claims in the application and patent which

define the same patentable invention as a count shall correspond to the count. At the time an interference is initiated (§ 1.611), a count shall not be narrower in scope than a claim that is patentable over the prior art and designated to correspond to the count or any patent claim designated to correspond to the count. Any single patent claim designated to correspond to the count shall be presumed, subject to a motion under § 1.633(c), not to correspond to the same patentable invention.

An interference may be declared between an application and a patent if the application and patent claim the same patentable invention, as defined in 37 CFR 1.601(n), and at least one of the applicant's claims to the invention are patentable to the applicant. Since one of the applicant's claims must be patentable, interference between an application and a patent may be declared if:

- (A) The patent is a reference against the application under 35 U.S.C. 102(b)/103;
- (B) The applicant's claims are not supported by the application disclosure, or otherwise do not meet 35 U.S.C. 112;
- (C) The applicant was not claiming the same or substantially the same invention as claimed in the application within 1 year after the date on which the patent was issued (35 U.S.C. 135(b); see also MPEP § 2307);
- (D) The patent is a reference against the application under 35 U.S.C. 102(e)/103, unless the applicant filed a showing under 37 CFR 1.608. See MPEP § 2307.02 concerning the rejection of claims in an application which correspond to claims of a patent.

Since the claims of a patent may not be altered (by reissue or reexamination), the applicant must claim the same patentable invention as is claimed in the patent. The applicant may add one or more claims of a patent in order to provoke an interference with the patent. The fact that the patent contains subject matter claimed by the applicant does not preclude interference if the patent does not claim the same subject matter.

The counts of the interference are formulated in essentially the same manner regardless of whether a patent or an application is involved. As stated in 37 CFR 1.601(n), a count shall define a separate patentable invention. Therefore, instead of having the same number of counts as copied patent claims, the examiner determines how many separate patentable inventions are claimed by the applicant and the patentee. When the interference is declared, there will be only one count for each separate patentable invention, with all the claims of the app

or after either is mailed from the Patent and Office. Additionally, the permanent record contains the appropriate patent number and the number. This record could be a separate or 37 CFR 1.607(d) notices sent to patentees appropriate identification of the patent and application.

arily, a 37 CFR 1.607(d) notice (Form para-
graph 20) is prepared by a person in the group having
charge over the application attempting to provoke
an interference with a patent. The original is placed of
the patented file, one copy is sent to the patentee.
An entry is made in the permanent group record
for 37 CFR 1.607(d) notices. If a final decision is made
to declare an interference will be declared, a primary examiner
will sign and file a 37 CFR 1.607(d) notice (Form
Paragraph 21).

The original of this notice is entered of record in the
patented file, one copy is sent to the patentee, and
an entry is made in the permanent record for
37 CFR 1.607(d) notices. If an interference is to be insti-
tuted, a declaration of interference notice will be sent
to the administrative patent judge and no additional form
is required by the examiner.

Through the permanent record for 37 CFR 1.607(d)
includes identification both of the patent and ap-
plicant. The patentee cannot and should not be given
any information concerning the party or application at-
tempting to provoke an interference unless and until an
interference is declared. 35 U.S.C. 122.

Interference Between an Application and a Patent; *Prima Facie* Showing by Applicant

2308. Interference between an application and a patent; *Prima Facie* showing by applicant.

- (1) When the effective filing date of an application is three months or less after the effective filing date of a patent, before an interference will be declared, either the applicant or the applicant's agent of record shall file a statement alleging that there is a basis upon which the applicant is entitled to a judgment relative to the application.
- (2) When the effective filing date of an application is more than three months after the effective filing date of a patent, the applicant, in order to declare an interference will be declared, shall file evidence which may consist of patents or printed publications, other documents, and one or more affidavits which demonstrate that applicant is *prima facie* entitled to a judgment relative to the patentee and an explanation stating with particularity the basis upon which the applicant is *prima facie* entitled to a judgment. Where the basis upon which an applicant is entitled to a judgment relative to a patentee is priority of invention, the evidence shall

include affidavits by the applicant, if possible, and one or more corroborating witnesses, supported by documentary evidence, if available, each setting out a factual description of acts and circumstances performed or observed by the affiant, which collectively would *prima facie* entitle the applicant to judgment on priority with respect to the effective filing date of the patent. To facilitate preparation of a record (§ 1.653(g)) for final hearing, an applicant should file affidavits on paper which is 21.8 by 27.9 cm. (8 1/2 x 11 inches). The significance of any printed publication or other document which is self-authenticating within the meaning of Rule 902 of the Federal Rules of Evidence or § 1.671(d) and any patent shall be discussed in an affidavit or the explanation. Any printed publication or other document which is not self-authenticating shall be authenticated and discussed with particularity in an affidavit. Upon a showing of good cause, an affidavit may be based on information and belief. If an examiner finds an application to be in condition for declaration of an interference, the examiner will consider the evidence and explanation only to the extent of determining whether a basis upon which the application would be entitled to a judgment relative to the patentee is alleged and, if a basis is alleged, an interference may be declared.

Under 37 CFR 1.608, an applicant seeking to provoke an interference with a patent is required to submit evidence which demonstrates that the applicant is *prima facie* entitled to a judgment relative to the patentee. Evidence must be submitted when the effective filing date of the application is more than 3 months after the effective filing date of the patent. The evidence may relate to patentability and need not be restricted to priority, but if the evidence shows that the claims of the application are not patentable, the claims in the application will be rejected. The applicant can file a request for reexamination of the patent, if applicable.

2308.01 Patent Has Filing Date Earlier Than Application

When an applicant attempts to provoke an interference with a patent, the examiner must determine the effective filing dates of the application and of the patent; only the patent's effective United States filing date will be considered. Any claim of foreign priority by the patentee under 35 U.S.C. 119 will not be taken into account when determining whether or not an interference should be declared, in order to be consistent with the holding in *In re Hilmer*, 359 F.2d 859, 149 USPQ 480 (CCPA 1966), that the effective date of a United States patent as a reference is not affected by the foreign filing date to which the patentee is entitled under 35 U.S.C. 119. If the patentee is determined to be entitled to the benefit of a prior United States application as to claimed subject matter involved in the interference, that application must be listed on the PTO-850 form (see MPEP § 2309).

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

BLACK BORDERS

IMAGE CUT OFF AT TOP, BOTTOM OR SIDES

FADED TEXT OR DRAWING

BLURRED OR ILLEGIBLE TEXT OR DRAWING

SKEWED/SLANTED IMAGES

COLOR OR BLACK AND WHITE PHOTOGRAPHS

GRAY SCALE DOCUMENTS

LINES OR MARKS ON ORIGINAL DOCUMENT

REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.